

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
10 May 2001 (10.05.2001)

PCT

(10) International Publication Number
WO 01/032217 A3

- (51) International Patent Classification⁷: A61K 9/50, 9/20 (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.
- (21) International Application Number: PCT/US00/30082
- (22) International Filing Date: 30 October 2000 (30.10.2000)
- (25) Filing Language: English
- (26) Publication Language: English (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- (30) Priority Data:
09/432,881 2 November 1999 (02.11.1999) US
- (71) Applicant: DEPOMED, INC. [US/US]; 1360 O'Brien Drive, Menlo Park, CA 94025 (US).
- (72) Inventors: MARKEY, Micheline; 2-3727 E. Cliff Drive No 5, Santa Cruz, CA 95062 (US). SHELL, John, W.; 952 Tournament Drive, Hillsborough, CA 94010 (US). BERNER, Bret; 239 El Granada Boulevard, El Granada, CA 94018 (US).
- (74) Agents: HEINES, M., Henry et al.; Townsend and Townsend and Crew LLP, 8th Floor, Two Embarcadero Center, San Francisco, CA 94111 (US).
- Published:
— with international search report
- (88) Date of publication of the international search report:
18 July 2002
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.



WO 01/032217 A3

(54) Title: PHARMACOLOGICAL INDUCEMENT OF THE FED MODE FOR ENHANCED DRUG ADMINISTRATION TO THE STOMACH

(57) Abstract: Drugs intended for absorption in the stomach or upper intestinal tract are administered in oral drug delivery systems in conjunction with any of various substances that have been discovered to function as potent agents for inducing the fed mode. By inducing the onset of the fed mode, these agents cause the stomach to prolong its retention of the drug delivery system, which is either large enough to be retained in the stomach during the fed mode or swells or expands to such a size upon ingestion. The fed mode inducing agents include the following compounds and their salts: glycine and glycylglycine, xylitol and related sugar alcohols, sodium and other metal docusates, β -casomorphins, α -lipoic acid and similarly structured acids, 2,2-diaryl-4-(4'-aryl-4'-hydroxypiperidino)butyramides, arginine, Trp-Trp, alkylpyridinium halides, dihydroxybenzoic acids, and potent sweeteners such as aspartame, aspartic acid, acesulfame, and stevioside.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/30082

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K9/50 A61K9/20

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, CHEM ABS Data, EMBASE, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>US 5 427 798 A (LUDWIG JENNIE SUE G ET AL) 27 June 1995 (1995-06-27)</p> <p>column 1, line 67 -column 2, line 12 column 2, line 40 -column 3, line 14 column 6, line 55 -column 7, line 16; example 1 claims 1-8</p> <p style="text-align: center;">--- -/--</p>	<p>1,2,5-9, 48-50, 97-99</p>

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

15 April 2002

Date of mailing of the international search report

25. 04. 2002

Name and mailing address of the ISA
European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.
Fax: (+31-70) 340-3016

Authorized officer

Muller, S

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/30082

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	EP 1 029 892 A (SUWELACK SKIN & HEALTH CARE AG) 23 August 2000 (2000-08-23) page 2, column 1, line 3 - line 10 page 3, column 4, line 19 -page 4, column 5, line 16 page 7, column 12, line 58 -column 13, line 21 page 8, column 14, line 34 -page 9, column 16, line 48 page 10, column 18, line 13 -column 19, line 4 claims 1-3,29,31,35-38,40-42 ---	1,2,5-9, 48,97-99
X	EFENTAKIS M; AL-HMOUND H: "The influence of surfactants on drug release from a hydrophobic matrix" INTERNATIONAL JOURNAL OF PHARMACEUTICS, vol. 70, no. 1-2, 1991, pages 153-158, XP001064514 page 154, column 1, line 35 -column 2, line 28 page 155, column 2; figure 2 ---	1,2, 38-42
X	EP 0 715 846 A (RHONE-POULENC RORER GMBH) 12 June 1996 (1996-06-12) page 7; example 5 ---	1,2, 5-13,47, 48,97-99
X	US 5 213 794 A (FRITSCH CHRISTIAN ET AL) 25 May 1993 (1993-05-25) column 3, line 55 - line 61 column 6 -column 7; example 2 ---	1,2,5,6, 10-13, 47,48, 97-99
X	US 4 871 546 A (FELTZ DENNIS R ET AL) 3 October 1989 (1989-10-03) column 1, line 14 - line 42 column 2 -column 3; example 1 ---	1,3-6, 14-16, 47,48, 52-54, 97-99
X	GB 1 330 829 A (SMITH KLINE FRENCH LAB) 19 September 1973 (1973-09-19) page 2, column 1, line 22 - line 47 page 3, column 1, line 52 -page 4, column 1, line 12 ----- -/--	1-8, 14-18, 47,97-99

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/30082

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>US 5 043 328 A (WEITHMANN KLAUS U) 27 August 1991 (1991-08-27)</p> <p>column 13 -column 14; examples 24,36 column 1, line 34 - line 38 column 16 -column 17; example 74 claim 1</p> <p style="text-align: center;">---</p>	<p>1,2,5,6, 23,24, 35-37</p>
X	<p>EP 0 571 217 A (MCNEIL PPC INC) 24 November 1993 (1993-11-24)</p> <p>page 9 -page 12; examples I,II figures 1-4 claims 1-10</p> <p style="text-align: center;">---</p>	<p>1-6, 27-31, 47-55, 97-99</p>
X	<p>US 4 470 980 A (HIGUCHI TAKERU ET AL) 11 September 1984 (1984-09-11)</p> <p>column 5 -column 7; examples 1,4,13,22,30,42 column 9; example 54 column 10, line 15 - line 21 claim 11</p> <p style="text-align: center;">---</p>	<p>1,2,5,6, 48,49, 97-99</p>
X	<p>STEPHENS J. AND CO: "Osmolyte and Tryptophan receptors controlling gastric emptying in the dog" AMERICAN JOURNAL OF PHYSIOLOGY, vol. 231, 1976, pages 848-853, XP001064412 cited in the application page 849, column 2, line 47 -page 850, column 1, line 4 page 850, column 2; figure 3 page 852, column 1, line 21 - line 30</p> <p style="text-align: center;">---</p>	<p>56-59</p>
A	<p>US 5 328 697 A (RAMAN SIVA N ET AL) 12 July 1994 (1994-07-12)</p> <p>column 1, line 40 - line 63 column 3, line 19 -column 5, line 14 column 5 -column 6; example 3 column 7 -column 8; examples 7,8 claims 1-3</p> <p style="text-align: center;">---</p>	<p>1-9, 32-34, 47-59, 82-84, 97-99</p>
A	<p>WO 99 25321 A (SMITHKLINE BEECHAM CORP ;VENKATESH GOPADI M (US)) 27 May 1999 (1999-05-27)</p> <p>page 10, line 30 -page 12, line 26; examples 5-7 claims 8,11,12</p> <p style="text-align: center;">---</p>	<p>1,2,5,6, 32-34, 48,49, 97-99</p>
	-/--	

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/30082

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WO 97 47285 A (DEPOMED INC ;SHELL JOHN W (US)) 18 December 1997 (1997-12-18) the whole document</p> <p>-----</p>	1-99

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/30082

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 56-96 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

As a result of the prior review under R. 40.2(e) PCT,
no additional fees are to be refunded.

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☒ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: partially claims 1-6,47-56,97-99,
entirely claims 7-9,32-34,57-59,82-84

- 1.1. Claims: partially claims 1-6,47-56,97-99,
entirely claims 7-9,57-59

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellaable polymer, and glycine, glycylglycine and salts thereof.

- 1.2. Claims: partially claims 1-6,47-56,97-99,
entirely claims 32-34,82-84

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellaable polymer, and arginine and arginine salts.

- 1.3. Claims: partially claims 1-6,47-56,97-99
A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellaable polymer, and aspartic acid and salts thereof.

2. Claims: partially claims 1-6,47-56,97-99,
entirely claims 10-13,60-63

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellaable polymer, and C4-C8 sugars alcohols.

3. Claims: partially claims 1-6,47-56,97-99,
entirely claims 14-18,64-68

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellaable polymer, and alkali and alkaline earth metal docusates.

4. Claims: partially claims 1-6,47-56,97-99,
entirely claims 19-22,69-72

FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellable polymer, and beta-casomorphins.

5. Claims: partially claims 1-6,47-56,97-99,
entirely claims 23-26,73-76

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellable polymer, and dithioorganic acids of formula X as defined in the present application.

6. Claims: partially claims 1-6,47-56,97-99,
entirely claims 27-31,77-81

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellable polymer, and
2,2-diaryl-4-(4'-aryl-4'-hydroxypiperidino)butyramides of formula X as defined in the present application.

7. Claims: partially claims 1-6,47-56,97-99,
entirely claims 35-37,85-87

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellable polymer, and the dipeptide Trp-Trp and salts thereof.

8. Claims: partially claims 1-6,47-56,97-99,
entirely claims 38-42,88-92

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellable polymer, and alkyl pyridinium halides of formula X as defined in the present application.

9. Claims: partially claims 1-6,47-56,97-99,
entirely claims 43-46,93-96

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellable polymer, and dihydroxybenzoic acids.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

10. Claims: partially claims 1-6,47-56,97-99

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellaable polymer, and stevioside.

11. Claims: partially claims 1-6,47-56,97-99

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellaable polymer, and alkyl esters of N-L-alpha-aspartyl L-phenylalanine.

12. Claims: partially claims 1-6,47-56,97-99

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellaable polymer, and 3,4-dihydro-1,2,3-oxathiazin-4-ones of formula X as defined in the present application.

Please note that all inventions mentioned under item 1, although not necessarily linked by a common inventive concept, could be searched without effort justifying an additional fee.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/30082

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5427798	A	27-06-1995	AT 161422 T	15-01-1998
			AU 677595 B2	01-05-1997
			AU 4725893 A	15-03-1994
			CA 2142320 A1	03-03-1994
			DE 69316015 D1	05-02-1998
			DE 69316015 T2	16-04-1998
			EP 0656775 A1	14-06-1995
			ES 2111168 T3	01-03-1998
			WO 9404138 A1	03-03-1994
			GR 3025794 T3	31-03-1998
			HK 1004323 A1	20-11-1998
			IL 106693 A	10-06-1997
			JP 8500110 T	09-01-1996
			LU 90656 A9	15-01-2001
			MX 9304967 A1	31-05-1994
			NZ 254947 A	26-04-1996
			SG 43911 A1	14-11-1997
			ZA 9305942 A	13-02-1995
EP 1029892	A	23-08-2000	EP 1029892 A1	23-08-2000
			AU 2802800 A	29-08-2000
			BR 0007472 A	16-10-2001
			CN 1340079 T	13-03-2002
			CZ 20012783 A3	13-03-2002
			WO 0047668 A1	17-08-2000
			NO 20013883 A	09-10-2001
EP 0715846	A	12-06-1996	DE 4444052 A1	13-06-1996
			AU 698749 B2	05-11-1998
			AU 3794795 A	20-06-1996
			CA 2164776 A1	11-06-1996
			EP 0715846 A1	12-06-1996
			JP 8208521 A	13-08-1996
			US 6024987 A	15-02-2000
			ZA 9510428 A	18-06-1996
US 5213794	A	25-05-1993	DE 4036757 A1	21-05-1992
			AT 127019 T	15-09-1995
			CA 2055536 A1	18-05-1992
			DE 59106367 D1	05-10-1995
			DK 486863 T3	27-12-1995
			EP 0486863 A1	27-05-1992
			ES 2077766 T3	01-12-1995
			GR 3017267 T3	30-11-1995
			JP 4290816 A	15-10-1992
			NONE	
US 4871546	A	03-10-1989	NONE	
GB 1330829	A	19-09-1973	AU 470023 B	04-03-1976
			AU 4230972 A	22-11-1973
			BE 783321 A1	10-11-1972
			CA 997677 A1	28-09-1976
			DE 2224390 A1	13-12-1973
			ES 402545 A1	01-04-1975
			FR 2138011 A5	29-12-1972
			IE 36335 B1	13-10-1976
			NL 7206328 A	21-11-1972
			ZA 7202664 A	31-01-1973

I. INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/30082

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5043328	A	27-08-1991	DE 3615710 A1	26-11-1987
			AT 77549 T	15-07-1992
			AU 603574 B2	22-11-1990
			AU 7264187 A	12-11-1987
			CA 1302266 A1	02-06-1992
			DE 3779958 D1	30-07-1992
			DK 235687 A	10-11-1987
			EP 0244832 A2	11-11-1987
			ES 2051705 T3	01-07-1994
			GR 3005768 T3	07-06-1993
			HU 44433 A2	28-03-1988
			IE 60273 B	29-06-1994
			IL 82459 A	31-07-1994
			JP 62267222 A	19-11-1987
			KR 9508306 B1	27-07-1995
			PT 84841 A ,B	01-06-1987
			ZA 8703299 A	02-11-1987
EP 0571217	A	24-11-1993	BR 1100507 A3	02-04-2002
			CA 2096575 A1	22-11-1993
			DE 69315257 D1	02-01-1998
			DE 69315257 T2	14-05-1998
			EP 0571217 A2	24-11-1993
			ES 2112387 T3	01-04-1998
			GR 93100197 A ,B	31-01-1994
			US 5599577 A	04-02-1997
			US 5679376 A	21-10-1997
			US 5716641 A	10-02-1998
			US 5980944 A	09-11-1999
US 4470980	A	11-09-1984	AT 29837 T	15-10-1987
			CA 1165690 A1	17-04-1984
			DE 3176461 D1	29-10-1987
			DK 101981 A	08-09-1981
			EP 0036534 A1	30-09-1981
			ES 500184 D0	01-12-1982
			ES 8301107 A1	16-02-1983
			FI 810637 A	08-09-1981
			GR 74441 A1	28-06-1984
			IE 52973 B1	27-04-1988
			JP 1495937 C	16-05-1989
			JP 56128714 A	08-10-1981
			JP 63046727 B	19-09-1988
			MX 6955 E	29-12-1986
			NO 810758 A ,B,	08-09-1981
			PT 72616 A ,B	01-04-1981
US 5328697	A	12-07-1994	AT 145552 T	15-12-1996
			AU 3661093 A	03-09-1993
			CA 2129754 A1	11-08-1993
			CN 1075253 A ,B	18-08-1993
			DE 69306243 D1	09-01-1997
			DE 69306243 T2	20-03-1997
			DK 625900 T3	02-06-1997
			EP 0625900 A1	30-11-1994
			ES 2095045 T3	01-02-1997
			JP 8502020 T	05-03-1996
			NZ 249658 A	28-05-1996

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/30082

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5328697	A	WO 9315725 A1	19-08-1993
WO 9925321	A	27-05-1999	
		AU 1588799 A	07-06-1999
		BR 9814877 A	03-10-2000
		CA 2310028 A1	27-05-1999
		CN 1285739 T	28-02-2001
		EP 1033974 A1	13-09-2000
		JP 2001522872 T	20-11-2001
		NO 20002526 A	16-05-2000
		PL 340587 A1	12-02-2001
		TR 200001412 T2	21-09-2000
		WO 9925321 A1	27-05-1999
WO 9747285	A	18-12-1997	
		AU 3290397 A	07-01-1998
		WO 9747285 A1	18-12-1997